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Similarities and differences in allocation policies for pediatric liver transplantation across the world

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Abstract

Objectives: We aimed to investigate national allocation policies for pediatric liver transplantation.

Method: A survey was prepared by the ESPGHAN hepatology committee in collaboration with the North-American SPLIT (Studies of Pediatric Liver Transplantation) consortium. The survey was sent to pediatric hepatologists and transplant surgeons worldwide. National data were obtained from centrally based registries.

Results: Replies were obtained from 15 countries from five of the world continents. Overall donation rate varied between 9 and 35 per million inhabitants. The number of pediatric liver transplantations was 4-9 per million inhabitants below 18 years of age for 13 of the 15 respondents. In children below 2 years of age mortality on the waiting list varied between 0 and 20%. In the same age group, there were large differences in the ratio of living donor liver transplantation to deceased donor liver transplantation as well as in the ratio of split liver segments to whole liver. These differences were associated with possible discrepancies in waiting list mortality.

Conclusion: Similarities but also differences between countries were detected. The described data may be of importance when trying to reduce waiting list mortality in the youngest children.

Keywords: Liver transplantation; allocation; waiting list; mortality; split liver; deceased donor; living donor

What is known

- Liver transplantation is a life saving treatment for children with severe liver disease.
- Stepwise innovations in surgical techniques have emerged in the last decades, increasing graft utilization for pediatric recipients

What is new

- Our survey suggests that while the rate of pediatric liver transplantations is quite similar between these 15 countries, there are important differences regarding organ donation rates, mortality on the waiting list for the youngest children, and the type of liver graft most commonly used.

Introduction

Liver transplantation (LT) is a life saving treatment for children with decompensated chronic liver disease, unresectable tumors, fulminant liver failure, and in some instances also for inherited metabolic conditions (1-2). Stepwise innovations in surgical techniques, living donor (LD) LT, as well as the use of reduced size or split grafts have emerged in the last decades, increasing graft utilization for pediatric recipients. Although these developments have increased the donor pool for children, all countries continue to face a gap between the demand and supply of organs from deceased donors and as a result, a relative shortage of grafts.

At the ESPGHAN monothematic conference on pediatric LT in 2013 geographic differences in organ allocation policies among countries were discussed (3). A review on global pediatric liver allocation recently summarized pediatric liver allocation policies in the United Kingdom, Spain, Italy, Eurotransplant and Switzerland, but to date there has been limited published descriptive data (4). We aimed to further delineate differences and impact of liver allocation policies to pediatric recipients in countries in Africa, Asia, Europe, North America, Oceania and South America. We focused on recipients below 2 years of age, since a large proportion of transplanted children, in particular those with biliary atresia, are in this age group (5-6) .

Method

A survey on national policies for organ allocation to pediatric LT was prepared by the ESPGHAN hepatology committee in collaboration with members of SPLIT (Studies of Pediatric Liver Transplantation) consortium. This survey was sent by e-mail to one designated pediatric hepatologist or transplant surgeon per participating country, who in turn collected and returned the data from centrally based registries in their own country

(supplementary table, Supplemental Digital Content, http://links.lww.com/MPG/B578). The respondents were asked to provide data for the latest 5 year period. The survey was distributed to a total of 17 countries in 2014, with a reminder in 2015. Details of the survey are available as supplementary material (Supplemental Digital Content, http://links.lww.com/MPG/B578).

Results

Replies were obtained from 15 countries representing five world continents (Table), i.e. from all surveyed countries except for Austria and Hungary. Details on demographics and allocation strategies are described in the same table. Children below 18 years of age comprised 16-37% of the total populations in each country. The number of centres per country performing pediatric LT varied between 1 and 56, the average number of pediatric LT per centre varied between 7 and 45. Five (33%) countries reported existing rules or incentives to always consider splitting the graft in donors below a certain age. PELD score or similar systems were used for allocation in 11 countries.

The overall donation rate varied between 2 and 35 per million inhabitants (Fig.1). The number of pediatric liver transplantations was 4-9 per million inhabitants below 18 years of age for 13 of the 15 respondents (Fig.2). It was considerably lower in South Africa (0.9 per million inhabitants below 18 years of age) and higher in Belgium (16.5 per million inhabitants below 18 years of age). For Belgium it should be noted that approximately 70% of pediatric liver recipients were from other countries, mainly young infants from Algeria, Israel, Russia, and Ukraine.

When looking more specifically at data available for children below 2 years of age, mortality on the waiting list (WL) varied between 0 and 20% (Fig.3). In the same age group, there were large differences between countries in the ratio of living donor (LD) LT to deceased donor

(DD) LT as well as in the ratio of split liver segments to whole liver (Fig.4-5). Survey results could define the following practice patterns:

a) Countries with at least two thirds receiving grafts from a live donor and less than one third transplanted with split organs from deceased donors (n=4).

b) Countries with at least two thirds receiving split organs from deceased donors and less than one third transplanted with a graft from a live donor (n=5).

c) Countries with a more even distribution between split organs from deceased organs and grafts from live donors (n=4).

d) USA, where only small numbers of patients received from split organs or live donors and a majority of the transplantations are performed with whole deceased donor livers.

Waiting list mortality in children below 2 years of age was low in groups a (range 0-8%) and b (0-4%) and higher in group c (9-20%), ($p=0.03$ for comparison of the combined groups a and b versus c, Mann-Whitney test) (Fig.6).

Discussion

We noted that the proportion of children to the whole population varied significantly among countries. On the other hand, the rate of pediatric liver transplantations per million children was with few exceptions quite stable, this despite the fact that these countries had obviously different allocation systems and strategies. One interpretation could be that each of these countries has independently arrived at a rather similar balance between transplant indication and organ availability. The diverging result from South Africa, with a much lower transplant rate, may suggest that a certain proportion of children in need of transplantation do not have access to the procedure.

The results of the present survey indicate that for children below 2 years of age there are striking differences between countries with regard to the ratio of LDLT to DDLT as well as in the ratio of split liver segments to whole liver. Furthermore, such large differences occur between countries of close geographic origin.

It was noted that Spain, which has the highest donation rate (Fig.1) belonged to group a. One explanation for this is that only pediatric cadaveric donors are allocated for pediatric candidates in non-urgent situations. The second reason is that there is no incentive to perform split liver transplantation.

Intention to treat survival for liver transplantation can be seen as the combination of WL survival and posttransplant survival (5-6). However, our survey was not aimed at detecting differences in the posttransplant outcome for the above mentioned types of transplantations. Other studies have arrived at diverging conclusions in this respect, but overall there might not be any substantial differences in long term posttransplant outcome. Interestingly, WL mortality seemed lower groups a and b than in group c. To reduce WL mortality, countries in group c might need to focus on increasing either the availability of split liver grafts or of living related liver transplantation for this age group. Such strategies, in particular an increased use of split liver grafts, would also be relevant when trying to reduce WL mortality in the US. As recently described, WL mortality is especially problematic in the sickest and youngest patients with biliary atresia, reinforcing the need to increase the potential donor pool (5-7)

The required rationing of deceased donor livers mandates the designation of allocation policies that dictate who is given priority for life-saving liver transplantation. Where do the rights of children fit into this model? In 1959, the United Nations General Assembly approved a resolution to protect the rights of the child, stating that “the child shall enjoy

special protection, and shall be given opportunities and facilities, by law and by other means, to enable him to develop physically, mentally, morally, spiritually, and socially in a healthy and normal manner…in the enactment of laws for this purpose, the best interests of the child shall be the paramount consideration" (8).

As expected, despite this mandate and others, owing to the wide variation of social, cultural and governmental structures worldwide, the answer to the ethical question of prioritizing children in the rationing of deceased donor organs manifests in an equally disparate fashion across continents.

This study has some obvious limitations. While we accumulated data on organ allocation and selection of recipients, information on important aspects such as access to organs and donor availability are lacking. Furthermore, our study delivers only a "snapshot" of the situation at a given time period. It does not take into account ongoing changes driven by for example national campaigns to increase donation or newer rules of incentives to always consider splitting organs from donors below a certain age. Although the study includes information from 15 countries spread around the world, data is unfortunately lacking for example from Asian countries with emerging programs for pediatric liver transplantation, such as India and Saudi Arabia (9-10). On the other hand, to the best of our knowledge, similar descriptive data collected from a widespread geographic combination of countries has not been published before. A future follow-up study would possibly show the dynamic development of these numbers over time. The combined efforts from SPLIT and the recently started European reference network for pediatric transplantation might prove useful to obtain data for such a study (11).

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Figure legends

Figure1 Donation rate per million inhabitants

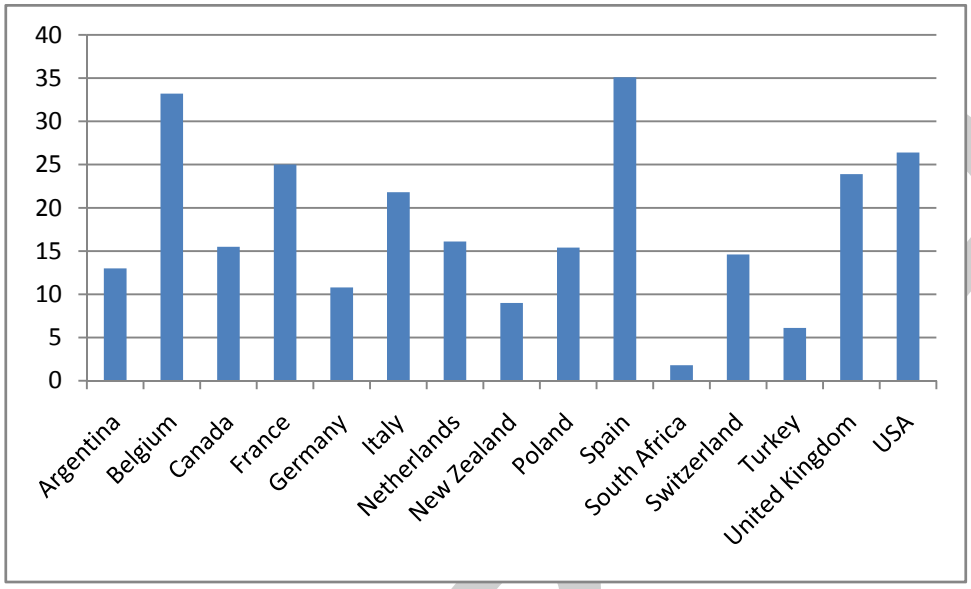
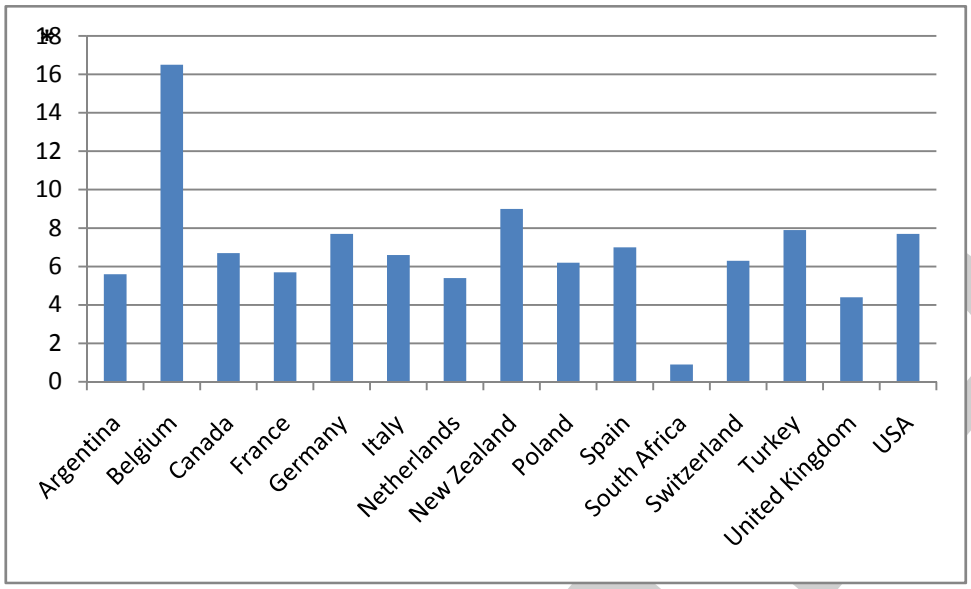
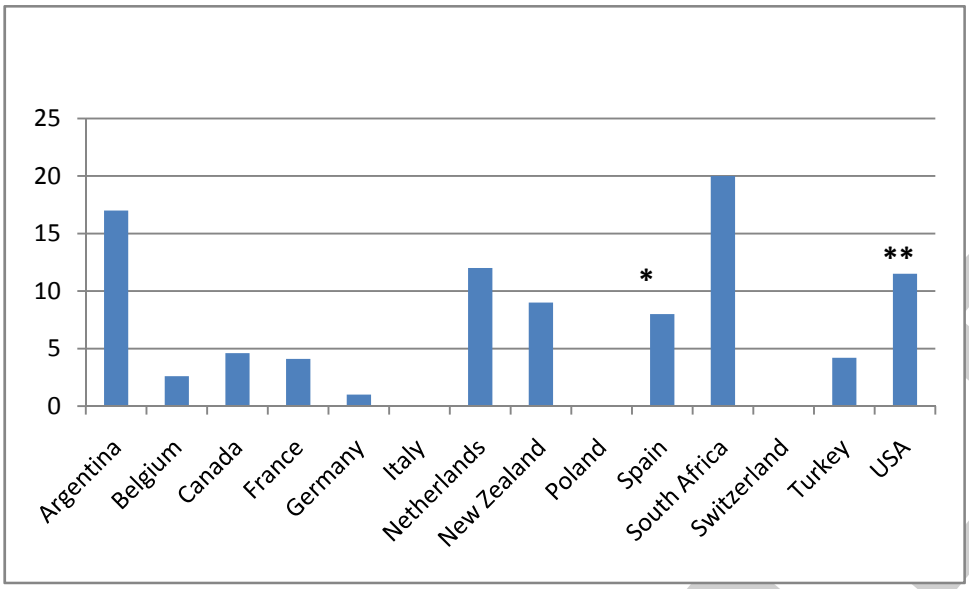


Figure 2 Pediatric liver transplantations per million inhabitants below 18 years of age



* 70% of the transplanted patients are from other countries

Figure 3 Waiting list mortality (%), children below 2 years of age.



* The data from Spain includes patients on waiting list for combined intestinal and liver transplantation.

** Data from USA reported for children below1 year of age.

Figure 4

Percentage of DDLT and LRLT in recipients below 2 years of age

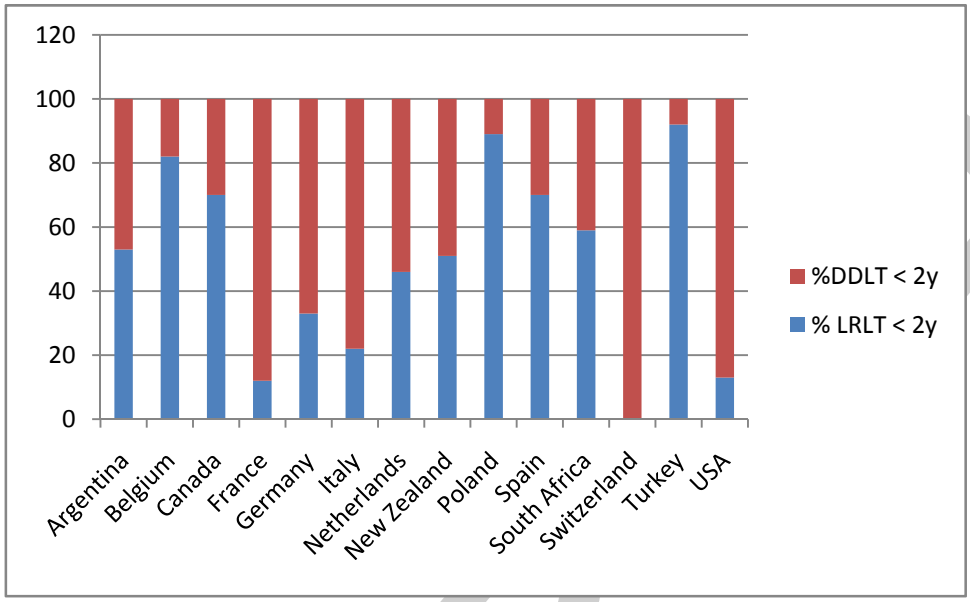


Figure 5 Type of organ in DDLT recipient below 2 years

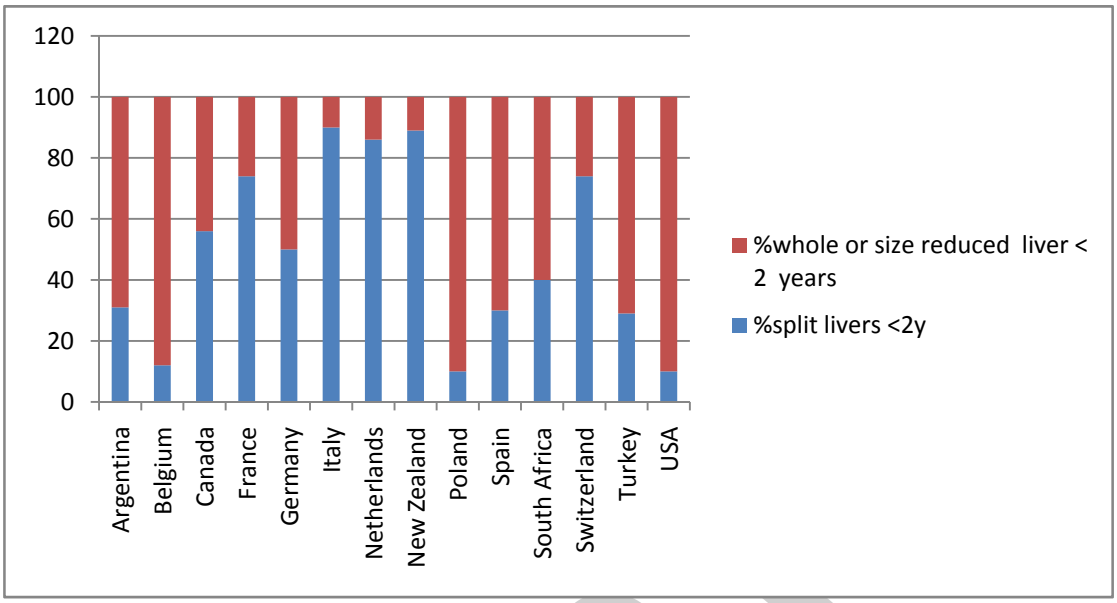
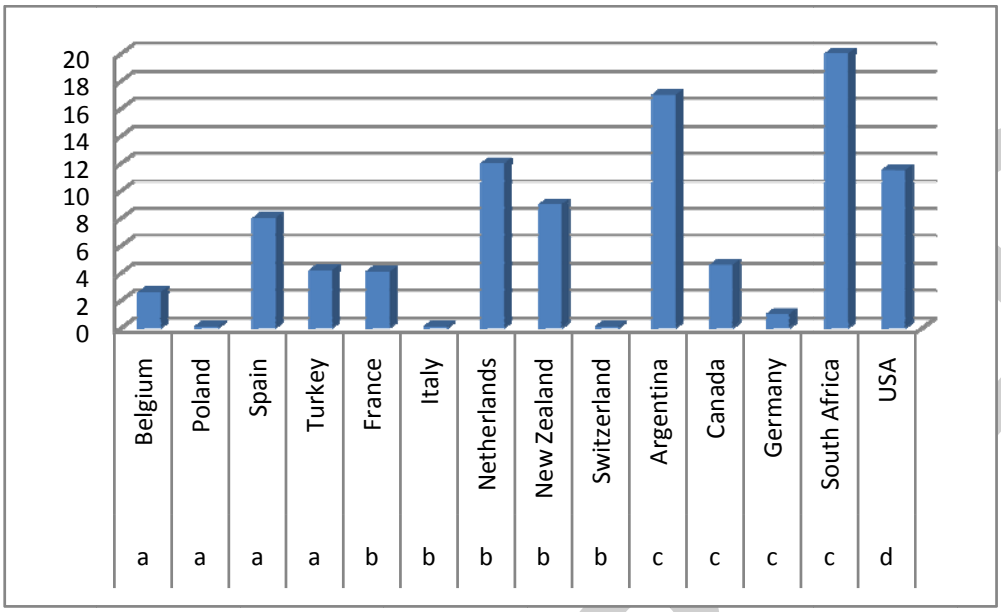


Figure 6. Waiting list mortality for children below 2 years of age in relation to pattern of allocation. For details, see also figure 3.



a) Countries with at least two thirds of such patients receiving grafts from a live donor and less than one third transplanted with split organs from deceased donors.

b) Countries with at least two thirds receiving split organs from deceased donors and less than one third transplanted with a graft from a live donor.

c) Countries with a more even distribution between split organs from deceased organs and live donors.

d) USA, where only small numbers of patients received from split organs or live donors and a majority of the transplantations are performed with whole deceased donor livers.